REMARKS

Claims 42, 43, 45-49, 53-59, and 61 are pending. Applicants thank the Examiner for withdrawal of the previous new matter rejection. Applicants respectfully request reconsideration of the claims in light of the following arguments. The Application is in a condition for allowance.

Claim Rejections – 35 U.S.C. § 102

Claims 42, 45, 47-49, 54, 59 and 61 were rejected under 35 U.S.C. § 102(e) as anticipated by Young *et al.* (WO 03/018040) in light of Dua *et al.* (*Br. J. Ophthalmol.* 1999) or Tseng (U.S. 6,152,142; IDS ref. #1). The Examiner stated that Young *et al.* teach a method and a composite graft for the treatment of conditions associated with photoreceptor loss (*e.g.*, age-related macular degeneration), where the composite graft comprising RPE cells is grown on base membrane such as amniotic membrane. 03/11/08 Office Action at 5. The Examiner also stated that Dua *et al.* teach that the amniotic membrane produces various growth factors and Young *et al.* teaches that amniotic membrane inherently comprises basement membrane and stroma.

Applicants traverse Examiner's § 102 rejection. Applicants invented the subject matter of the claims at issue prior to the effective date of Young *et al.*, August 2001. *See* 37 C.F.R. § 1.131 Declarations of Drs. Scheffer C.G. Tseng and Susanne Binder, attached herewith. Applicants also wish to bring to the Examiner's attention that the earliest Young application claiming priority to August 2001, U.S. 60/314,911, does not even disclose the use of amniotic membrane at all. However, Applicants' date of invention clearly precedes even this date. *See id.* Neither Dua *et al.* or Tseng contain all the elements of the claims. In light of the attached 1.131 Declarations, Examiner's § 102 rejection over Young *et al.* in light of Dua or Tseng should be withdrawn.

Claim Rejections – 35 U.S.C. § 103

Young et al.

Claims 42, 43, 45-49, 57-59 and 61 were rejected under 35 U.S.C § 103(a) as unpatentable over Young *et al.* (*supra*). Applicants traverse Examiner's § 103(a) rejection for the same reasons in response to Examiner's § 102 rejection over Young et al. above. Applicants invented the subject matter of the claims at issue prior to the effective date of Young *et al.*, August 2001. *See* Tseng and

Binder Declarations. In light of the attached 1.131 Declarations, Examiner's § 103(a) rejection over Young *et al.* should be withdrawn.

Young et al. in view of Grueterich et al.

Claim 53 was rejected under 35 U.S.C § 103(a) as unpatentable over Young *et al.* in view of Grueterich *et al.* (2002; IDS ref. #28). As before, Applicants traverse Examiner's § 103 rejection for the following reasons. Applicants invented the subject matter of the claims at issue prior to the effective date of Young *et al.*, August 2001. *See* Tseng and Binder Declarations. Applicants also invented the subject matter of the claims at issue prior to the effective date of Grueterich *et al.*, January 2002. *See id.* In light of the attached 1.131 Declarations, Examiner's § 103 rejection over Young *et al.* in view of Grueterich *et al.* should be withdrawn.

Young et al. in view of Tseng

Claims 54-58 were rejected under 35 U.S.C § 103(a) as unpatentable over Young *et al.* in view of Tseng. As before, Applicants traverse Examiner's § 103 rejection for the following reasons. Applicants invented the subject matter of the claims at issue prior to the effective date of Young *et al.*, August 2001. *See* Tseng and Binder Declarations. Tseng on its own does not teach the limitations of claim 42. In light of the attached 1.131 Declarations, Examiner's § 103 rejection over Young *et al.* in view of Tseng should be withdrawn.

Liu in view of Dutt et al. in further view of Dua et al. and Young et al.

Using a 4-way combination of art (which should be evidence in itself of non-obviousness), Claims 42, 43, 45-46, 49, 54, 57-59 and 61 were rejected over Liu (U.S. 6,045,791; IDS ref. #7) in view of Dutt *et al.* (1991; IDS ref. #15) in further view of Dua *et al.* and Young *et al.* The Examiner further defines the term "confluent" to mean anything from just above 0% coverage to 100% coverage in order bring this 4-way combination into line with Applicants' claims.

Applicants traverse Examiner's § 103 rejection for the following reasons. First, a skilled artisan would not have been motivated to replace the collagen substrate of Liu with the amniotic membrane of Dutt *et al.* because the amniotic membrane of Dutt *et al.* is incapable of achieving confluent RPE cells or confluent RPE equivalent cells on the membrane, as required by the claims.

With all due respect, the only way to breathe any relevance into Dutt *et al.* is to devise a novel definition of "confluent": which is precisely what the Examiner has done. The Examiner posits that "[w]ith regard to the term 'confluent,' since it does not define the amount of confluence (*e.g.* 50% or 100%, etc.), the term is considered as any percentage of confluence for RPE cells." 03/11/08 Office Action at 5 (emphasis added). However, this definition is inconsistent with the instant specification and the ordinary meaning of "confluent." A fraction of coverage would be non-confluent or subconfluent, which by definition is not confluent. Further, "percentage of confluence" as the Examiner contemplates makes no sense. As an analogy, one would not interpret the term "filled" to mean 10% filled, 50% filled, and 75% filled; nor would one interpret the term "finished" to mean 10% finished, 50% finished, and 75% finished.

As Applicants have repeatedly pointed out in prior responses, the claims of the present Application require a confluent culture. A "confluent" cell culture as used in the art is one in which the cells are in contact over the entire growth surface of the culture vessel. *See, e.g.*, Harrison & Rae, *General Techniques of Cell Culture* (1997), page 69 (confluent when "cells are touching each other and there is no more substrate space"); Pollard & Walker, *Basic Cell Culture Protocols* (1997), page 17 (confluent when the "culture surface is completely covered with cells"). Further, this common understanding of "confluent" is contemplated by the Application. *See* Application, ¶ [0073] (distinguishing "subconfluent" from "confluent"). The term "confluent" in the claims should therefore be interpreted according to this ordinary and customary meaning. M.P.E.P. § 2111.01 (stating that the words of a claim take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art).

A claim must be read to give each term effect. *See Texas Instruments Inc. v. U.S. Int'l Trade Comm'n*, 988 F.2d 1165 (Fed. Cir. 1993) (stating that express limitations should not be read out of the claims). Because the Examiner's interpretation of "confluence" is not aligned with the ordinary and customary meaning, and would effectively vitiate the word in the claim, the Examiner's novel and unprecedented definition should not be adopted. Indeed, the Examiner's interpretation of "confluence" renders the term meaningless, since "confluent" cells could mean anything from just above 0% coverage to 100% coverage.

Therefore, the Examiner is incorrect that "the amniotic membrane [of Dutt *et al.*] can be used for the same purpose as the collagen substrate [of Liu]." The Examiner does not dispute that the RPE

cells grown on the amniotic membrane of Dutt do not cover the entire growth surface (*i.e.*, are non-confluent). *See* 03/11/08 Office Action at 2. In light of the ordinary meaning of "confluent" as used in the art and as contemplated by the Application, the amniotic membrane of Dutt *et al.* is not inferior, but incapable of achieving confluent RPE or RPE equivalent cells as required by the claims, and one of skill in the art would not combine Liu and Dutt to achieve the claimed invention.

Further, Dua does not resolve the deficiencies of Liu in view of Dutt. Dua discloses the use of amniotic membrane in the eye, but does not teach that amniotic membrane can be used for the same purpose as the collagen substrate of Liu for achieving confluent RPE or RPE equivalent cells as required by the claims. The Examiner's rejection over Young *et al.* must also be withdrawn because Applicants invented the subject matter of the claims at issue prior to the effective date of Young *et al.*, August 2001. *See* Tseng and Binder Declarations. Therefore, the Examiner's rejection using the 4-way combination of Liu (U.S. 6,045,791; IDS ref. #7) in view of Dutt *et al.* (1991; IDS ref. #15) in further view of Dua *et al.* and Young *et al.* should be withdrawn in its entirety.

Liu in view of Dutt in further view of Dua et al., Young et al., and Grueterich et al.

Claim 53 was rejected under 35 U.S.C § 103(a) using the **5-way combination** of Liu in view of Dutt *et al.* in further view of Dua *et al.*, Young *et al.*, and Grueterich *et al.* The Examiner's rejections over Young *et al.* and Grueterich *et al.* must be withdrawn because Applicants invented the subject matter of the claims at issue prior to the effective date of Young *et al.*, August 2001. *See* Tseng and Binder Declarations.

Applicants respectfully traverse Examiner's rejection for the same reasons as stated above in Applicant's arguments that Claims 42, 43, 45-46, 49, 54, 57-59 and 61 are not obvious over Liu in view of Dutt *et al.* in further view of Dua *et al.* Therefore, the Examiner's rejection over Liu in view of Dutt *et al.* in further view of Dua *et al.*, Young *et al.*, and Grueterich *et al.* should be withdrawn in its entirety.

CONCLUSION

Applicant submits that this paper fully addresses the Office Action mailed March 11, 2008. Applicant respectfully solicits the Examiner to expedite prosecution of this patent application to allowance. Should the Examiner have any questions, the Examiner is encouraged to contact the undersigned attorney at (858) 350-2306. The Commissioner is authorized to charge any additional fees that may be required, including petition fees and extension of time fees, or credit any overpayment to Deposit Account No. 232415 (Docket No.: 34157-707.831).

Respectfully submitted,
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